

Initial clinical experience with the Strut-Adjusted Volume Implant brachytherapy applicator for accelerated partial breast irradiation

Catheryn M. Yashar^{1,*}, Sarah Blair², Anne Wallace³, Dan Scanderbeg¹

¹Department of Radiation Oncology, University of California San Diego, La Jolla, CA

²Department of Surgery, Division of Surgical Oncology, University of California San Diego, La Jolla, CA

³Department of Surgery, Divisions of Plastics and Surgical Oncology, University of California San Diego, La Jolla, CA

ABSTRACT

PURPOSE: Accelerated partial breast irradiation is becoming increasingly popular. The Cianna single-entry high-dose-rate applicator, Strut-Adjusted Volume Implant (SAVI, Cianna Medical, Aliso Viejo, CA), contains peripheral struts allowing greater planning flexibility for small-breasted women, technically easier insertion, and normal tissue exposure minimization. This study evaluates early clinical experience.

METHODS AND MATERIALS: Thirty patients treated with the SAVI with a median followup of 12 months were evaluated. The median age was 59.5. Tumor size averaged 0.9 cm. Fifteen cancers were ductal carcinoma in situ (50%), 1 was invasive lobular (3.3%), 4 were tubular (6.7%), and the rest infiltrating ductal (40%). Most of them were estrogen receptor (ER) positive (90%). Nine women (30%) were premenopausal.

RESULTS: Dosimetry was outstanding with median V90, V150, and V200 of 96.2%, 24.8, and 12.8 cc. There were no symptomatic seromas, and one report of asymptomatic fat necrosis seen on mammogram at 1 year. In patients who had skin spacing of less than 1 cm, the median skin dose was 245 cGy/fraction. The median rib and lung dose per fraction for those patients with either structure less than 1 cm was 340 and 255 cGy (75% of prescribed dose), respectively. There have been no local recurrences to date.

CONCLUSIONS: Early clinical experience with the SAVI demonstrates the ease of placement of a single-entry brachytherapy device combined with the increased dose modulation of interstitial brachytherapy. Dose to normal structures has remained exceedingly low. Almost half of evaluated patients were not candidates for other single-entry brachytherapy devices because of skin spacing or breast size, demonstrating an expansion of candidates for single-entry partial breast brachytherapy.

© 2009 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords:

Accelerated partial breast irradiation; SAVI; Breast brachytherapy; Breast cancer

Introduction

Since the inception of breast conservation, whole breast irradiation (WBI), usually with daily treatment for 5–6 weeks, has been the standard of care demonstrating excellent local control in prospective, randomized studies with greater than 20 years of followup (1, 2). Recently, investigators have questioned the need to treat the entire breast,

as review of prior data demonstrates that most failures occur near the original tumor bed, and failures remote from the tumor bed are not affected by WBI (3–5). These observations stimulated investigation into the utility and efficacy of partial breast irradiation. With partial breast irradiation treating a smaller volume of breast tissue, investigation also turned to treating women with a more accelerated course of therapy completing treatment in 5 days, thus termed accelerated partial breast irradiation (APBI). Initial studies used low-dose-rate multicatheter interstitial brachytherapy (IBT) and subsequently have transitioned to high-dose-rate treatment (6–17). This early research demonstrated that, in a properly selected patient population, APBI prevented ipsilateral breast cancer recurrence as effectively as WBI with ≥5-year followup (18–20). In these reports, cosmesis

Received 11 February 2009; received in revised form 24 March 2009; accepted 26 March 2009.

* Corresponding author. Department of Radiation Oncology, University of California San Diego, Moores Cancer Center, 3855 Health Sciences Drive #0843, La Jolla, CA 92093-0843. Tel.: +1-858-822-6059; fax: +1-858-822-5568.

E-mail address: cyashar@ucsd.edu (C.M. Yashar).

is good to excellent in most of the patients and toxicity has been minimal (21, 22). Hungary has recently published the first randomized prospective trial comparing WBI to APBI. With a median followup of 5 years, this study again demonstrates equivalent control of APBI when compared with WBI and superior cosmetic outcome (23). Currently, there is an ongoing randomized, prospective trial sponsored by the National Cancer Institute, the National Surgical Adjuvant Breast and Bowel Project (NSABP-39), and the Radiation Therapy Oncology Group (0413) randomizing eligible women between WBI and APBI using one of three methods: IBT, MammoSite (RTS Cytotec Corp., Marlborough, MA) brachytherapy, or 3D conformal therapy.

Despite published data on IBT, APBI was not widely used in the United States until appearance of the MammoSite catheter, a single-entry balloon device. Since the introduction of MammoSite, several studies have published data reporting the equivalency of MammoSite APBI to WBI with ≥ 5 -year followup, in a nonrandomized fashion (24–28). In addition, there has been investigation of 3D conformal external beam irradiation to accomplish the same APBI goal (29).

Despite these various methods to deliver APBI, it is not universally available to women who are candidates based on pathologic criteria alone. Interstitial breast brachytherapy is technically challenging and not taught in most North American Radiation Oncology residency programs, so many physicians are ill-equipped to offer this alternative. MammoSite brachytherapy, although technically and dosimetrically less challenging, excludes those women with small breasts and tumor beds close to the skin, secondary to excessive normal tissue toxicity and poor cosmesis (24, 30). Recent reports have also demonstrated increased rib fractures with MammoSite brachytherapy (31). In addition, with 3D conformal therapy, the target volume must occupy less than 30% of the whole breast volume, and beams should not traverse the contralateral breast, enter/exit directly into the heart, or include excessive lung volume. These considerations leave many women, especially small-breasted women or those with tumors in the inner quadrants or other extremes of the breast, ineligible for APBI.

To surmount these exclusions and allow more women the option of APBI, the Strut-Adjusted Volume Implant (SAVI, Cianna Medical, Aliso Viejo, CA) was developed (Fig. 1). This breast brachytherapy device combines the ease of the single-entry device with the flexibility of IBT while still treating the minimal tissue necessary for APBI. It comes in 3 sizes, with 7, 9, or 11 struts available for ^{192}Ir loading, allowing for expansive dose modulation near normal tissues, such as the skin, chest wall, and heart (32).

Methods and material

From November 2006 until June 2008, a total of 30 patients completed treatment with the SAVI breast



Fig. 1. Strut-Adjusted Volume Implant device.

brachytherapy device at the University of California San Diego after lumpectomy and axillary lymph node evaluation. This study is a retrospective review of those patients, and Institutional Review Board approval was obtained for this project. Criteria for treatment included invasive breast cancer or ductal carcinoma in situ, tumor size ≤ 3 cm, age ≥ 18 years, node negative, and final margins negative per NSABP definition. Exclusion criteria included multicentricity or positive margins. There were no exclusion criteria for normal tissue proximity. The patient characteristics are presented in Table 1.

SAVI placement was performed by the surgeon or radiation oncologist with the closed cavity technique. Entrance to the lumpectomy site was either through the lumpectomy scar (scar entry technique) or through a separate 1 cm incision on an outpatient basis under local anesthesia with or without anxiolysis. Prophylactic antibiotics were used at the discretion of the treating physician. Computed tomography (CT) imaging was then performed for assurance of full strut deployment, symmetry, appropriateness of SAVI size chosen, and tumor bed proximity to skin and chest wall. The same CT was used for treatment planning. The CT images were then imported into the PLATO planning system (Nucletron B.V., Veenendaal, Netherlands). The tumor bed was then outlined by the treating physician and the struts digitized with the planning software. For detailed technical information, please see prior published guidelines (32). A dose of 34 Gy in 10 twice daily fractions was prescribed 1 cm from the edge of the tumor bed. Each fraction was separated from the prior fraction by at least 6 h. Before each fraction, orthogonal films were obtained to monitor for device

Table 1
Patient characteristics

Age	Median, 59.5 (41–77)
Tumor histology	Infiltrating ductal, 12 (40%) Tubular, 2 (6.7%) Infiltrating lobular, 1 (3.3%) Ductal carcinoma in situ, 15 (50%)
Multifocality	4 (13%)
Tumor size	Median, 9 mm; mean, 9.8 mm; range, 2 mm–3 cm
Menopause status	Premenopausal, 9 (30%)
Hormonal status	ER positive, 27 (90%)
Her 2 neu status	Negative, 28 (96%) Unknown, 1 (3.3%)
Other therapies	None, 11 (40%) Hormonal, 15 (50%) Chemo, 2 (6.6%) (1 patient with chemo and hormonal manipulation) Unknown, 2 (6.6%)

rotation or displacement. If position appeared to be altered, a full CT of the device was performed. If there was any question of device movement, especially if the device was close to the skin or chest wall, replanning was performed. After the final treatment, the device was removed and the incision dressed with steri-strips.

The patients were followed every 3–4 months. An ipsilateral baseline mammogram was ordered at 6 months post-treatment and then resumption of bilateral mammograms began at a year. The MRIs were ordered at the discretion of the treating oncologists. Followup examinations included a history and physical noting breast edema, erythema, fibrosis, hyperpigmentation, hypopigmentation, telangiectasias, and fat necrosis. The patient symptoms were also recorded. Toxicities were graded using the Common Toxicity Criteria, version 2.0 (33). Breast cosmesis was scored according to the Harvard criteria (34). The patients were treated with chemotherapy, hormonal manipulation, or both at the discretion of the treating oncologists.

Results

The median follow has been 12 months (range, 5–21 months). The age range of patients is 41–77 years, with a median of 59.5 years. One device was removed and not used for a full treatment schedule secondary to infection. All deployments of remaining devices were adequate for treatment, and no device had to be pulled for unsatisfactory placement, skin or chest-wall distance, or air gaps outside the device. Clinical diagnosis of infection was seen in 6% of treated patients with 80% given antibiotics either prophylactically or for treatment of suspected infection. One patient developed an eschar at the insertion site, but this was felt to be a surgical wound as the skin did not fall into the high-dose radiation region. This area healed with a small skin retraction.

Dosimetry has been excellent with median V90 of 96.2% (82–99.6%), V150 of 24.8 cc (range,

8.2–40.6 cc), and V200 of 12.8 cc (range, 3.7–18.7 cc). The median skin dose for all the patients was 252 cGy/fraction (74%) (range, 45–367 cGy). Skin to tumor bed edge distances ranged from 1 to 42 mm, with a mean distance of 11.46 mm. For those patients with skin spacing less than 1 cm, 13 patients, the median skin dose per fraction was 245 cGy (72%) (range, 217–285 cGy). The median rib and lung dose per fraction for those patients with spacing of either less than 1 cm was 340 and 255 cGy (75%), respectively (ranges, 242–510 cGy and 195–400 cGy, respectively). Replanning at anytime after insertion secondary to changes in catheter positioning was necessary in 9 out of the 30 patients. Five patients were replanned before the first fraction (within the first 24 h after insertion) leaving 4 (13%) with changes in position during the first week of the treatment. After replanning, old plans were recast on new CTs and only 1 patient in the four replans had a drop in V90% to less than 90% indicating a necessity for replanning. Because it takes the same amount of time to recast a plan on a new CT, the default is to replan.

In a followup, 1 patient developed keloids at both the lumpectomy site and the SAVI insertion site. Cosmesis has been good to excellent in all the patients with no persistent edema, erythema, fibrosis, hyperpigmentation, hypopigmentation, breast pain, or telangiectasias. No symptomatic persistent seromas were reported. One case of asymptomatic fat necrosis at the 18-month followup mammogram was reported. There have been no local recurrences.

Conclusion

For women who fit the pathologic criteria, APBI is becoming a more acceptable, attractive, and available method of treatment. In North America, IBT is not widely available, nor are Radiation Oncologists universally trained in this method. The MammoSite catheter facilitated the ease of placement and planning of breast brachytherapy and quickly increased the popularity of APBI. MammoSite has some serious limitations, however. Small-breasted women may not be candidates for the MammoSite balloon primarily because of dose limitations of the normal tissues, most notably skin (24, 30). Despite the lack of clinical data regarding full dose to adjacent ribs, lungs, and at times heart, the relative inability to modulate the dose to these normal structures is a critical drawback (31). In addition, women whose tumor bed lies within 7 mm of the skin are not candidates for MammoSite brachytherapy because of acute and chronic skin toxicity when exposed to the unmodulated dose. On the open NSABP B-39 trial, many of the enrolled patients randomized to APBI have chosen 3D conformal irradiation and this remains the preference, and in fact the only option, for many centers. However, not all women are candidates for 3D conformal radiation. Small-breasted women are likely excluded as with

MammoSite as guidelines stipulate that the planning target volume (PTV) must represent less than 30% of the breast volume. In addition, depending on the site of the tumor bed relative to normal tissues, some tumor beds cannot be adequately covered without radiation beams traversing critical organs, such as lung, heart, shoulder, or the contralateral breast. There have also been several reports that this accelerated external beam schedule may cause unexpected normal tissue side effects, such as radiation pneumonitis, pericarditis, and increased tissue fibrosis, over other APBI techniques (35, 36). Although these reports are preliminary, caution must be exercised before the publication of the prospective randomized trial.

To address these concerns and expand the population of women eligible for APBI, Cianna Medical developed the single-entry, multichannel breast brachytherapy device, SAVI. This study describes the first 30 patients treated with the device at the University of California, San Diego. Although median followup is still short, the SAVI device has been successfully used to treat a wider population of women eligible for APBI. In fact, 33.3% of the women treated at this institution would not have been eligible for MammoSite brachytherapy because of skin-spacing restriction (<7 mm).

Insertion has been successfully completed with only one device removed for florid infection before treatment completion. The median V90, V150, and V200 fall well within NSABP B-39 guidelines and in fact fall closer to the MammoSite guidelines than interstitial (Table 2). These guidelines were easily achievable while maintaining a maximum skin dose $\leq 100\%$ of the prescribed dose, even when the device was within 5 mm of the skin (Figs. 2 and 3). Chest wall, rib, and lung doses were also maintained below 80% of the prescribed dose in all women and many had simultaneous skin and chest-wall restrictions, speaking to the versatility of the device (Fig. 4). In this regard, the removal for normal tissue proximity is unnecessary with the SAVI device as radiation modulation to minimize normal tissue dose is a strength of the design. Deployment of the device was simple with no need for removal due to air gaps, poor positioning, or inability to treat the target tissue. Positioning of the device was stable and although daily orthogonal films were used for daily quality assurance, the need for replanning was minimal.

Table 2
Comparison of NSABP B-39 guidelines and SAVI values

	NSABP B-39 guidelines MammoSite	NSABP B-39 guidelines interstitial	SAVI, median (range)
V90%	$\geq 90\%$ PTV evaluation	$\geq 90\%$ PTV evaluation	96.2% (82–99.6%)
V ₁₅₀	≤ 50 cc	≤ 70 cc	24.8 cc (8.2–40.6 cc)
V ₂₀₀	≤ 10 cc	≤ 20 cc	12.8 cc (3.7–18.7 cc)

NSABP = National Surgical Adjuvant Breast and Bowel Project; PTV = planning target volume; SAVI = Strut-Adjusted Volume Implant.

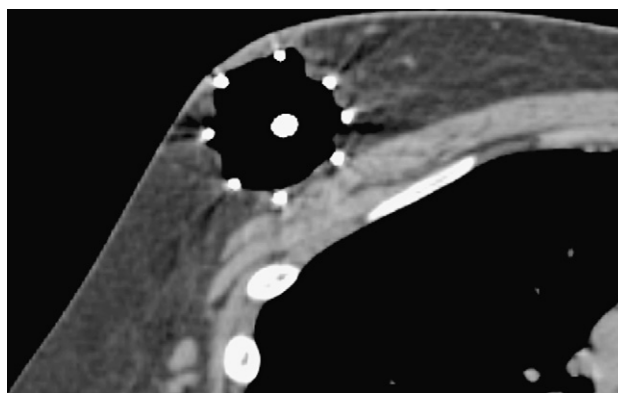


Fig. 2. Demonstration of Strut-Adjusted Volume Implant with very close skin margin.

Infection rate was low (2%), with 80% of women treated with prophylactic antibiotics. The patient discomfort was minimal with most devices placed on an outpatient basis under local anesthesia with or without anxiolysis, and the removal has been done without additional anesthesia. Cosmesis has been excellent with one keloid formation at the SAVI insertion site and lumpectomy scar. There has been no hyperpigmentation, edema, erythema, or telangiectasias. There have been no reports of symptomatic persistent seroma and one report of asymptomatic fat necrosis at 18 months to date. Six percent of women received adjuvant chemotherapy and 40% received adjuvant hormonal manipulation. One patient received both, and 40% of patients received no further therapy. The ipsilateral and contralateral recurrence rate has been 0%, although follow-up is short.

For eligible patients, the SAVI breast brachytherapy device allows simple outpatient insertion and improved dose modulation to conform to patient anatomy. The added versatility not only increases patient eligibility, but may also decrease normal tissue toxicity when compared with other single-entry devices or 3D conformal therapy. This study represents the first clinical report on the use of the

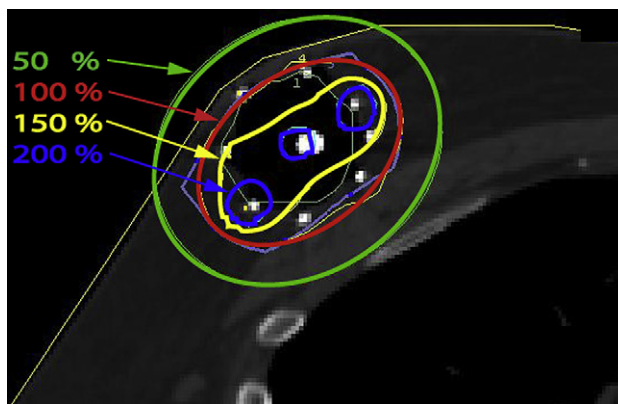


Fig. 3. Isodose lines of Strut-Adjusted Volume Implant with close skin margin demonstrating ability to keep skin dose low.

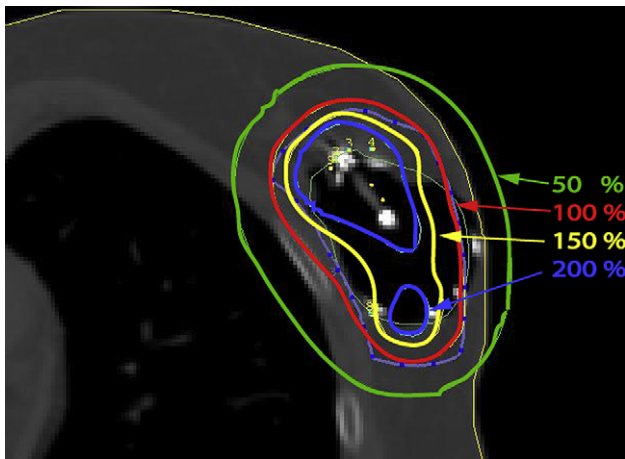


Fig. 4. Strut-Adjusted Volume Implant close to both skin and chest wall.

device and, although followup remains short, the clinical outcome has been outstanding with excellent cosmetic results, little morbidity, and no local recurrences.

References

- [1] Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233–1241.
- [2] Veronesi U, Cascinelli N, Mariani L, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 2002;347:1227–1232.
- [3] Fowble B. Ipsilateral breast tumor recurrence following breast-conserving surgery for early stage invasive cancer. *Acta Oncol Suppl* 1999;13:9–17.
- [4] Veronesi U, Luini A, del Vecchio M, et al. Radiotherapy after breast preserving surgery in women with localized cancer of the breast. *N Engl J Med* 1993;328:1587–1591.
- [5] Fowble B, Soli LJ, Schultz DJ, et al. Breast recurrence following conservative surgery and radiation: Patterns of failure, prognosis, and pathologic finding from mastectomy specimens with implications for treatment. *Int J Radiat Oncol Biol Phys* 1990;19:833–842.
- [6] Arthur DW, Doo D, Swicker RD, et al. Partial breast brachytherapy after lumpectomy: Low-dose-rate and high-dose-rate experience. *Int J Radiat Oncol Biol Phys* 2003;56:681–689.
- [7] Baglan KL, Martinez AA, Frazier RC, et al. The use of high-dose-rate brachytherapy alone after lumpectomy in patients with early-stage breast cancer treated with breast-conserving therapy. *Int J Radiat Oncol Biol Phys* 2001;50:1003–1011.
- [8] Krishnan L, Jewell WR, Tawfik OW, et al. Breast conservation therapy with tumor bed irradiation alone in a selected group of patients with stage I breast cancer. *Breast J* 2001;7:91–96.
- [9] Perera F, Yu E, Engel J, et al. Patterns of breast recurrence in a pilot study of brachytherapy confined to the lumpectomy site for early breast cancer with six years' minimum follow-up. *Int J Radiat Oncol Biol Phys* 2003;57:1239–1246.
- [10] Polgár C, Major T, Fodor J, et al. High-dose-rate brachytherapy alone versus whole breast radiotherapy with or without tumor bed boost after breast-conserving surgery: Seven-year results of a comparative study. *Int J Radiat Oncol Biol Phys* 2004;60:1173–1181.
- [11] Ott OJ, Hildebrandt G, Pötter R, et al. Accelerated partial breast irradiation with multi-catheter brachytherapy: Local control, side effects and cosmetic outcome for 274 patients. Results of the German-Austrian multi-centre trial. *Radiother Oncol* 2007;82:281–286.
- [12] Ott OJ, Pötter R, Hammer, et al. Accelerated partial breast irradiation with Iridium-192 multicatheter PDR/HDR brachytherapy: Preliminary results of the German-Austrian multicenter trial. *Strahlenther Onkol* 2004;180:642–649.
- [13] Strnad V, Ott OJ, Pötter R, et al. Interstitial brachytherapy after breast conserving surgery: Interim results of a German-Austrian multicenter phase II trial. *Brachytherapy* 2004;3:115–119.
- [14] Vicini FA, Arthur DW. Breast brachytherapy: North American experience. *Semin Radiat Oncol* 2005;15:108–115.
- [15] Vicini FA, Kestin L, Chen P, et al. Limited-field radiation therapy in the management of early-stage breast cancer. *J Natl Cancer Inst* 2003;95:1205–1211.
- [16] Wazer DE, Berle L, Graham R, et al. Preliminary results of a phase I/II study of HDR brachytherapy alone for T1/T2 breast cancer. *Int J Radiat Oncol Biol Phys* 2002;53:889–897.
- [17] Arthur DW, Winter K, Kuske RR, et al. A Phase II trial of brachytherapy alone after lumpectomy for select breast cancer: Tumor control and survival outcomes of RTOG 95-17. *Int J Radiat Oncol Biol Phys* 2008;72:467–473.
- [18] King TA, Bolton JS, Kuske RR, et al. Long-term results of wide-field brachytherapy as the sole method of radiation therapy after segmental mastectomy for T(is1,2) breast cancer. *Am J Surg* 2000;180:299–304.
- [19] Fa Vicini, Baglan KL, Kestin LL, et al. Accelerated treatment of breast cancer. *J Clin Oncol* 2001;19:1993–2001.
- [20] Polgár C, Sulyok Z, Fodor J, et al. Sole brachytherapy of the tumor bed after conservative surgery for T1 breast cancer: Five-year results of a phase I-II study and initial findings of a randomized phase III trial. *J Surg Oncol* 2002;80:121–128.
- [21] Chen PY, Vicini FA, Benitez P, et al. Long-term cosmetic results and toxicity after accelerated partial-breast irradiation: A method of radiation delivery by interstitial brachytherapy for the treatment of early-stage breast carcinoma. *Cancer* 2006;106:991–999.
- [22] Kuske RR, Winter K, Arthur DW, et al. Phase II trial of brachytherapy alone after lumpectomy for select breast cancer: Toxicity analysis of RTOG 95-17. *Int J Radiat Oncol Biol Phys* 2006;65:45–51.
- [23] Polgár C, Fodor J, Major T, et al. Breast-conserving treatment with partial or whole breast irradiation for low-risk invasive breast carcinoma—5-Year results of a randomized trial. *Int J Radiat Oncol Biol Phys* 2007;69:694–702.
- [24] Benitez PR, Keisch ME, Vicini F, et al. Five-year results: The initial clinical trial of Mammosite balloon brachytherapy for partial breast irradiation in early-stage breast cancer. *Am J Surg* 2007;194:457–462.
- [25] Vicini F, Beitsch P, Quiet C, et al. Two year analysis of treatment efficacy and cosmesis by the American Society of Breast Surgeons (ASBS) MammoSite Breast Brachytherapy Registry Trial in patients treated with accelerated partial breast irradiation (APBI). *J Clin Oncol* 2006;18S:529.
- [26] Cuttino LW, Arthur DW, Keisch M, et al. Multi-institutional experience using the MammoSite Radiation Therapy System (RTS) in the treatment of early-stage breast cancer: 2 Year results. *Int J Radiat Oncol Biol Phys* 2006;66:S30–S31.
- [27] Prestidge B, Sadeghi A, Rosenthal A, et al. Local control of early stage breast cancer using MammoSite HDR brachytherapy. *Int J Radiat Oncol Biol Phys* 2006;66: S215.
- [28] Chao K, Vicini F, Wallace M, et al. Analysis of treatment efficacy, cosmesis and toxicity using the MammoSite breast brachytherapy catheter to deliver accelerated partial breast irradiation: The William Beaumont Hospital experience. *Int J Radiat Biol Oncol Phys* 2007;69:32–40.
- [29] Vicini FA, Chen P, Wallace M, et al. Interim cosmetic results and toxicity using 3D conformal external beam radiation therapy to deliver accelerated partial breast irradiation in patients with early-stage breast cancer treated with breast-conserving therapy. *Int J Radiat Oncol Biol Phys* 2007;69:1124–1130.

- [30] Dragun AE, Harper JL, Jenrette JM, et al. Predictors of cosmetic outcome following MammoSite breast brachytherapy: A single-institution experience of 100 patients with two years of follow-up. *Int J Radiat Oncol Biol Phys* 2007;68:354–358.
- [31] Brashears JH 3rd, Dragun AE, Jenrette JM. Late chest wall toxicity after MammoSite(R) breast brachytherapy. *Brachytherapy* 2009;8: 19–25.
- [32] Scanderbeg D, Yashar C, Rice R, et al. Clinical implementation of a new HDR brachytherapy device for partial breast irradiation. *Radiother Oncol* 2009;90:36–42.
- [33] Trotti A, Byhardt R, Stetz J, et al. Common toxicity criteria: Version 2.0. An improved reference for grading the acute effects of cancer treatments: Impact on radiotherapy. *Int J Radiat Oncol Biol Phys* 2000;47:13–47.
- [34] Rose MA, Olivetto I, Cady B, et al. Conservative surgery and radiation therapy for early breast cancer. Long-term cosmetic results. *Arch Surg* 1989;124:153–157.
- [35] Recht A, Ancukiewicz M, Lu X, et al. Lung dose-volume parameters and the risk of pneumonitis for patients treated with accelerated partial-breast irradiation (APBI) using 3D conformal radiotherapy (3D-CRT). *Int J Radiat Oncol Biol Phys* 2008;72. S4.
- [36] Hepel J, Tokita M, MacAusland S, et al. Toxicity of 3D-CRT for accelerated partial breast irradiation. *Int J Radiat Oncol Biol Phys* 2008;72. S5.